

AMENDMENT TO THE SPECIFICATION

Please replace paragraphs [0066], [0070], [0077], [0084], and [0151] of the specification as filed with the following replacement paragraphs:

[0066] The ratio of the total lead particles : the aggregation-inhibiting substance ~~to the total lead particles~~ in the method of inhibiting aggregation of complex particles in which a drug is adhered to the lead particles of the present invention is preferably 1:0.9 to 1:0.01, more preferably 1:0.7 to 1:0.1, further more preferably 1:0.6 to 1:0.2, the most preferably 1:0.5 to 1:0.3 in ratio by weight.

[0070] The ratio of the lead particles to the liquid in which the lead particles are dispersed is not particularly limited as long as the drug A or the drug A and the adhesion-competitive agent can be adhered to the lead particles, however, it is preferably 1 $\mu\text{g/mL}$ to 1 g/mL , more preferably 0.1 to 500 mg/mL . Further, in the step of dispersing or dissolving the drug A or the drug A and the adhesion-competitive agent so as to be contained in the liquid in which the lead particles containing the aggregation-inhibiting substance are dispersed, when a liquid in which the drug A or the drug A and the adhesion-competitive agent is/are dispersed or dissolved is added to the liquid in which the lead particles are dispersed, the ratio of the total amount of the drug A and the adhesion-competitive agent to the liquid in which the drug A or the drug A and the adhesion-competitive agent is/are dispersed or dissolved is not particularly limited as long as the drug A or the drug A and the adhesion-competitive agent can be adhered to the lead particles, however, it is preferably 1 $\mu\text{g/mL}$ to 1 g/mL , more preferably 0.1 to 400 mg/mL . The ratio of the lead particles : the total amount of the drug A and the adhesion-competitive agent ~~to the lead particles~~ are preferably 1:1 to 1000:1, more preferably 2:1 to 200:1 in ratio by weight.

[0077] Further, examples of the lipid to be used in the case where the coating layer is a lipid membrane include a synthetic lipid and the like. Examples of the synthetic lipid include fluorinated phosphatidylcholine, a fluorinated surfactants, dialkylammonium bromide and the like. These may be used alone or in combination with another lipid or the like. Further, in the case where the coating layer is a lipid membrane, the coating layer preferably contains a water-

soluble polymer derivative. Examples of the water-soluble polymer derivative include the lipid derivatives or the fatty acid derivatives of a water-soluble polymer illustrated in the above-mentioned definition of the aggregation-inhibiting substance and the like, and preferred examples include the polyethylene glycolated phospholipids illustrated in the above-mentioned definition of the aggregation-inhibiting substance and the like. Further, the water-soluble polymer derivative is preferably a substance having a dual character that a part of the molecule has a property of binding to the aggregation-inhibiting substance or the adhesion-competitive agent in the present invention due to, for example, hydrophilic affinity, electrostatic force or the like, and other part has a property of binding to other coating layer components due to, for example, hydrophobic affinity, electrostatic force or the like. By using such a substance, the efficiency of the coating of the complex particles of the present invention is increased. The ratio of the total coating layer components : the water-soluble polymer derivative ~~to the total coating layer components~~ is preferably 1:0.5 to 1:0.01, more preferably 1:0.25 to 1:0.01, further more preferably 1:0.15 to 1:0.02 in ratio by weight.

[0084] The ratio of the complex particles of the present invention to be used in the method of producing coated complex particles of the present invention to the liquid A and the liquid B is not particularly limited as long as it allows the complex particles to be coated with the coating layer component, however, it is preferably 1 µg/mL to 1 g/mL, more preferably 0.1 to 500 mg/mL. Further, the ratio of the coating layer component (such as a lipid) to be used to the liquid A and the liquid C is not particularly limited as long as it allows the complex particles of the present invention to be coated, however, it is preferably 1 µg/mL to 1 g/mL, more preferably 0.1 to 400 mg/mL. The ratio of the complex particles : the coating layer component ~~to the complex particles~~ of the present invention is preferably 1:0.1 to 1:1000, more preferably 1:1 to 1:10 in ratio by weight.

[0151] As can be seen from Table 8, in any of the preparations obtained in Examples 20 to 27, the recovery rate of EPC is high, and coating of the complex particles with the coating lipid was efficiently carried out. Further, the preparations obtained in Examples 21, 22, 25 and 26, in which the total coating layer components : the ratio of the water-soluble polymer derivative ~~to~~

~~the total coating layer components~~ is 1:0.25 to 1:0.01 in ratio by weight, were more preferred because the average particles diameters of the coated fine particles were smaller, and the recovery rates of EPC were higher.